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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/690,973	10/18/2000	Spiridon Spireas	MPCI-0024	4370

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[REDACTED] EXAMINER

WARE, TODD

[REDACTED] ART UNIT [REDACTED] PAPER NUMBER

1615

DATE MAILED: 01/15/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/690,973	SPIREAS, SPIRIDON	
	Examiner	Art Unit	
	Todd D Ware	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) Responsive to communication(s) filed on 21 February 2002.
- 2a) This action is FINAL. 2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) Claim(s) 1-92 is/are pending in the application.
- 4a) Of the above claim(s) 24-77 and 80-89 is/are withdrawn from consideration.
- 5) Claim(s) _____ is/are allowed.
- 6) Claim(s) 1-23, 78, 79 and 90-92 is/are rejected.
- 7) Claim(s) _____ is/are objected to.
- 8) Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on _____ is/are: a) accepted or b) objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) The proposed drawing correction filed on _____ is: a) approved b) disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) All b) Some * c) None of:
1. Certified copies of the priority documents have been received.
2. Certified copies of the priority documents have been received in Application No. _____.
3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
a) The translation of the foreign language provisional application has been received.
- 15) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- | | |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) <u>11</u> | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Receipt of supplemental information disclosure statement filed 5-6-02 and amendment/response filed 10-23-02 is acknowledged. Claims 78-79 have been amended as requested and new claims 90-92 have been added. Claims 1-92 are pending.

Election/Restrictions

1. This application contains claims 24-77 and 80-89 drawn to an invention nonelected with traverse in Paper No. 9, filed 2-1-02. A complete reply to the final rejection must include cancelation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.
3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.
4. Claims 8 and 19 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.
5. Claims 8 and 19 do not use Markush language and the claim is indefinite because it is unclear whether all the ingredients are excipients in the formulation or if

each ingredient is a separate member of a group of excipients. Amendment with "selected from the group consisting of" would overcome this rejection. See MPEP 2173.05(h). For purposes of examination, the claims are examined as such.

Response to Arguments

6. Applicant's arguments filed 10-23-02 have been fully considered but they are not persuasive. Applicant argues that one of ordinary skill understands that the list of species and phrase "or combination thereof" indicates that any individual species or a combination of the species is the excipient in the formulation. This argument is not found persuasive. As written, the claim fails to set forth species since it does not recite Markush language. As written, each of the 7 elements is included as an excipient. Indefiniteness occurs upon inclusion of the phrase "or combination thereof" because all 7 elements are already included as a combination. For purposes of examination, the previous Office Action was on the basis that the phrase "or combination thereof" implies that Applicant intended to claim each individual element as a species in a Markush group. The rejection is maintained since these claims still do not recite language identifying Markush groups. Applicant's statement that the claim language suggested in the previous Office Action is not consistent with the scope of Applicant's invention is not understood. It is the position of the examiner that the phrase "or combination thereof" would be permitted in the claims and cover combination of elements, should Markush language be recited.

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

8. Claims 1-2, 4-8, 10-13, 15-19, 21-23, and 78-79 rejected under 35 U.S.C. 102(b) as being clearly anticipated by Chen et al (5,225,204; hereafter '204).

'204 discloses levothyroxine capsule powder formulations with hydroxypropyl methylcellulose (abstract; C 3, L 28-32, 68; C 5, L 1-29, L 52-54; Example1 & 3; claims).

Response to Arguments

9. Applicant's arguments filed 10-23-02 have been fully considered but they are not persuasive. Applicant argues that '204 does not disclose that the formulations are prepared under conditions that avoid the exacerbation of moisture induced degradation, i.e. conditions of low compression, and points to Example 2 of '204. This argument is not found persuasive, since this is only one embodiment of '204. '204 also discloses granulation of a levothyroxine formulation where the formulation is then dried and passed through a mesh screen and then placed in capsules. The instant claims do not set forth any requirements for setting forth what constitutes a low pressure other than dependent claims stating that the pressure is not more than a claimed psi/g (e.g. instant claims 5-7). Furthermore, it is well established that claims are given the broadest interpretation during examination (In re Bozek 163 USPQ 545; In re Kerich 96 USPQ 411; Heyer v. Brenner, Comr. Pats. 146 USPQ 3). '204 does not disclose that this process is performed under additional pressure to that of atmospheric pressure, it is

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therefore understood that this process occurs under at most atmospheric pressure which is interpreted as meeting the limitation since this pressure is not more than the claimed (that is dependent claims e.g. instant claims 5-7) psi/g.

Claim Rejections - 35 USC § 103

10. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

11. Claims 1-2, 4-13, 15-23, 78-79, and 90-92 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chen et al (5,225,204; hereafter '204).

'204 teaches levothyroxine capsule powder formulations with hydroxypropyl methylcellulose (abstract; C 3, L 28-32, 68; C 5, L 1-29, L 52-54; Example1 & 3; claims). '204 does not specifically state that the residual moisture content should be less than about 10% by weight, however it would have been obvious to one skilled in the art at the time of the invention with the motivation of maximizing stability of the levothyroxin and the expectation that levothyroxin degrades rapidly under conditions of high humidity (C 1, L 32-35; C 2, L 32-35; C 3, L 10-15; C 5, L 52-54).

Response to Arguments

12. Applicant's arguments filed 10-23-02 have been fully considered but they are not persuasive. Applicant argues that '204 does not teach that the formulations are prepared under conditions that avoid the exacerbation of moisture induced degradation,

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i.e. conditions of low compression, and points to Example 2 of '204. This argument is not found persuasive, since this is only one embodiment of '204. '204 also discloses granulation of a levothyroxine formulation where the formulation is then dried and passed through a mesh screen and then placed in capsules. The instant claims do not set forth any requirements for setting forth what constitutes a low pressure other than dependent claims stating that the pressure is not more than a claimed psi/g (e.g. instant claims 5-7). Furthermore, it is well established that claims are given the broadest interpretation during examination (In re Bozek 163 USPQ 545; In re Kerich 96 USPQ 411; Heyer v. Brenner, Comr. Pats. 146 USPQ 3). '204 does not disclose that this process is performed under additional pressure to that of atmospheric pressure, it is therefore understood that this process occurs under at most atmospheric pressure which is interpreted as meeting the limitation since this pressure is not more than the claimed (that is dependent claims e.g. instant claims 5-7) psi/g. Furthermore, '204 explicitly teaches that the invention of '204 is to provide a stabilized formulation of levothyroxine having a long shelf life under a variety of storage conditions. Accordingly, absent data, the instant claims do not appear to provide a formulation that is critically different from that of the prior art.

13. Claims 1-2, 4-13, 15-23, 78-79, and 90-92 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chen et al (5,225,204; hereafter '204) in view of Mitra (5,955,105; hereafter '105).

'204 is relied upon for all that it teaches as stated previously. '204 does not specifically teach that the residual moisture content should be less than about 10% by weight.

'105 is relied upon for teaching levothyroxine formulations having a moisture content less than 4.5% provide maximum stability of levothyroxine.

Accordingly, it would have been obvious to one skilled in the art at the time of the invention to combine '204 and '105 with the motivation of providing maximum stability of the formulation.

Response to Arguments

14. Applicant's arguments filed 10-23-02 have been fully considered but they are not persuasive. Since Applicant's arguments are primarily on the basis that the primary reference is deficient and the secondary references do not cure the deficiencies of the primary references, the Response to Arguments *supra* paragraph 12 is again relied upon.

15. Claims 1-23, 78-79, and 90-92 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chen et al (5,225,204; hereafter '204) in view of Sarkar (4,001,211; hereafter '211) or Chen et al (5,225,204; hereafter '204) in view of Yamamoto et al (5,756,123; hereafter '123).

'105 is relied upon for all that it teaches as stated previously. '105 does not teach the limitations where the capsule shell is formed of hydroxypropyl methylcellulose.

'211 and '123 both teach capsule shells comprising hydroxypropyl methylcellulose

Accordingly, it would have been obvious to one skilled in the art at the time of the invention to use capsule shells formed of hydroxypropyl methylcellulose in the formulation of '105 with the motivation of providing capsules that are stable under humid conditions and that do not lose their ability to degrade under particular conditions.

Response to Arguments

16. Applicant's arguments filed 10-23-02 have been fully considered but they are not persuasive. Since Applicant's arguments are primarily on the basis that the primary reference is deficient and the secondary references do not cure the deficiencies of the primary references, the Response to Arguments *supra* paragraph 12 is again relied upon.

17. Claims 1, 5-12, 16-23, 78-79, and 90-92 are rejected under 35 U.S.C. 103(a) as being unpatentable over of Mitra (5,955,105; hereafter '105) in view of Schor et al (4,389,393; hereafter '393) or Mitra (5,955,105; hereafter '105) in view of Maish et al (4,983,399; hereafter '399).

'105 teaches levothyroxine formulations having a moisture content less than 4.5% provide maximum stability of levothyroxine. '105 doesn't specifically teach the instant limitations requiring no compression greater than 2,000 psi/g, 5,000 psi/g or 10,000 psi/g.

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'393 and '399 both teach that formulations compressed at 2,000 psi/g, 5,000 psi/g or 10,000 psi/g are well-known in the art.

Accordingly, it would have been obvious to one skilled in the art at the time of the invention to compress the formulations of '105 at these pressures with the motivation of obtaining a tablet with a desired hardness, friability, and disintegration time.

Response to Arguments

18. Applicant's arguments filed 10-23-02 have been fully considered but they are not persuasive. Applicant argues that '393 and '399 do not teach low compression, since the compression pressures (e.g. 2,000 to 16,000 lbs/in²) are meaningless without knowing the mass of the tablet being compressed and '393 teaches tablets having a mass of less than one gram. Applicant then continues that the compression pressure of Example 6 ('393) results in 6,973.5 psi/gram. While this pressure is greater than the 5,000 psi/gram as required in instant claims 6 and 17, page 11, lines 10-12 of the instant specification professes that "conditions of low compression" are those not in excess of about 10,000 psi/g and Applicant has not set forth the criticality of pressures less than this amount. Moreover, '105 recognizes the significance of low moisture in regards to stability in thyroid hormone formulations and that applicant has argued that the instant invention is ultimately directed toward avoidance of moisture induced degradation of thyroid hormone. It therefore appears that '105 recognizes this importance of having a low moisture content.

Conclusion

19. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

20. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Todd D Ware whose telephone number is (703) 305-1700. The examiner can normally be reached on M-F, 8:30 AM - 5 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman K Page can be reached on (703)308-2927. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4556 for regular communications and (703) 308-4556 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1234.

tw
January 11, 2003

THURMAN K. PAGE
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